REMARKS

Claims 1-24 are pending in the application. Claims 1-24 have been rejected. Claims 3-10 and 17 have been cancelled, and claims 1, 2, 11, 23 and 24 have been amended. New claims 25-37 have been added. The amendments to the specification, claims and the incorporation of new claims are editorial in nature and contain no new matter. Therefore, Applicants respectfully request entry of the Amendment.

CLAIM OBJECTIONS

In the Office Action, the Examiner objected to Claim 17 as being a duplicate of claim 16. Applicants have herein cancelled Claim 17, and accordingly request that the Examiner withdraw his objection.

CLAIM REJECTIONS - 35 U.S.C. § 112 SECOND PARAGRAPH

In the Office Action, the Examiner asserted that claims 1-24 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to " a substantially pure polysaccharide preparation".

Applicants respectfully disagree. In the specification, Applicants have indicated that (page 7, lines 4-6),

> " a substantially pure preparation means a preparation in which the total dry weight of the polysaccharide of the invention is at least 60 % of the total dry weight, exclusive of the weight of other intentionally included compounds".

Applicants further describe at lines 10-13:

> " Thus, if the polysaccharides of the invention are mixed with one or more other compounds (e.g. diluents, detergents, excipients, salts, sugars, lipids) for purposes of administration, stability, storage, and the like, the weight of such other compounds is ignored in calculation of the purity of the preparation."

Based on this description, Applicants assert that it would be understood by anyone skilled in the art that substantially pure polysaccharide preparations, should not include a consideration of the inclusion of excipients and the like in the preparation, rather, in terms of the active component of the composition, the polysaccharide preparation.

The Examiner further rejected use of the term "enriched" in reference to the polysaccharide preparations of this invention, as failing to provide metes and bounds to what is encompassed in the preparation. Applicants have herein amended the claims to refer to compositions comprising heparin polysaccharides obtained by treatment of heparin sulfate with 3-OST-3, and methods utilizing polysaccharide preparations thus obtained. Applicants have stated in the specification, at page 5, lines 9-13:

> "The polysaccharide preparations of the invention are enriched for 3-OST-3 sulfated polysaccharides approximately 10-100 fold. Whereas the percentage of 3-OST-3 sulfated polysaccharide in a typical unenriched preparation is less than 0.1 %, the percentage of 3-OST-3 sulfated polysaccharide in the enriched polysaccharide preparations of the invention is about 5 – 7 %."

Thus, Applicants have provided the metes and bounds of the polysaccharide preparations, beyond comprising only "a measurable amount of 3-O-sulfated glucosamine", as indicated by the Examiner. Accordingly, Applicants request withdrawal of the rejection.

CLAIM REJECTIONS - 35 U.S.C. § 102

In the Office Action, the Examiner rejected claims 1-19 under 35 U.S.C. § 102(b), as allegedly being anticipated by Casu et al.

Applicants respectfully disagree. Casu describes chemically sulfated glycosaminoglycans, which have high antithrombotic activity (Specification at page 3, lines 1-2, and lines 29-30, and Page 6, lines 15-18), with exemplification for only 6-O-sulfated heparin sulfate polysaccharides, and not 3-O-sulfated polysaccharides.

The claimed invention is directed to, however, use of a 3-OST-3 enzyme to produce 3-O-sulfated glucosamine residues in the heparin polysaccharides. Utilization of the 3-OST-3 enzyme produces a preparation substantially enriched specifically for 3-O-sulfated glucosamine residues, irrespective of the 6-O sulfation state of the heparin polysaccharide, as disclosed in Casu. The methods/preparations taught by Casu, cannot provide for preferential 3-O-sulfation.

Moreover, the heparin polysaccharides obtained in Casu et al, are claimed as being useful as antithrombotics, whereas heparin sulfate polysaccharides contacted with 3-OST-3 do not have significant antithrombotic activity, characteristic instead of polysaccharides which have been contacted with 3-OST-1, the latter polysaccharides exhibiting poor activity in binding Herpes virus gD-1. Thus, Casu does not teach the heparin sulfate polysaccharides comprising 3-O-sulfated glucosamine residues, obtained via contacting a heparin polysaccharide with a 3-OST-3 enzyme, as claimed in the subject Application.

Accordingly, Applicants respectfully request withdrawal of the rejection.

CLAIM REJECTIONS - 35 U.S.C. § 103

In the Office Action, the Examiner rejected claims 1-19 as being rendered obvious in view Rosenberg et al.

Applicants respectfully disagree. It would not be obvious to one skilled in the art, based on Rosenberg et al that there is a difference between the use of 3-OST enzymes to generate sulfated heparin polysaccharides, for treating HSV infection. Applicants have demonstrated that 3-OST-3, and not 3-OST-1 provide for substantial inhibition of HSV

infection. Thus, Rosenberg et al, did not teach pharmaceutical preparations comprising specifically 3-OST-3 treated heparin polysaccharides, nor have such preparations been rendered obvious, as based on Rosenberg, it would not have been obvious that 3-OST-3 treated heparin polysaccharides would specifically bind HSV gD, and inhibit infection, the finding of the instant invention. Accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner rejected claims 1, 20-22 and 24 as being rendered obvious in view of Lukas (US patent No. 4, 465,666) further in view of Casu (WO 98/42754) or Rosenberg (WO 99/22005) and Lycke et al (J. Gen. Virol., 1991).

Applicants claim a method of inhibiting herpes simplex virus type- I (HSV- 1) viral infection comprising administering a therapeutically effective amount of a pharmaceutical composition comprising a substantially pure Heparin Sulfate polysaccharide preparation enriched for IdoA2S-GIcN3S residues to a mammal diagnosed with HSV- I infection (claim 24), and the pharmaceutical preparation thus generated (claim 1-22).

The Examiner alleged that Lukas et al teaches the use of heparin to inhibit Herpes virus infection, however use of heparin alone, without zinc did not appreciably inhibit HSV infection, while its combination with zinc was effective in inhibiting HSV infection, therefore Lukas does not appear to teach the efficacy of heparin sulfate polysaccharides in inhibiting HSV infection, and certainly does not teach, nor render obvious, the use of 3-OST-3 treated heparin sulfate polysaccharides for inhibiting HSV infection.

The Examiner alleged that Casu teaches the 3-O-sulfated heparin polysaccharides used in Applicants invention. As stated hereinabove, Casu describes glycosaminoglycans, ***which have high antithrombotic activity***, moreover, Casu does not provide for preferenctial 3-O-sulfation, which is obtainable via the methods of this invention, and in the preparations thus obtained. Thus, Casu does not teach, nor render obvious, the heparin sulfate

polysaccharides comprising 3-O-sulfated glucosamine residues of the subject Application, nor does its combination with Lukas teach the unexpected finding of the instant invention that 3-OST-3 treated heparin sulfate polysaccharides bind HSV gD, and inhibit HSV infection.

The Examiner alleged that Lycke teaches that heparin and highly sulfated heparin inhibits cellular attachment of HSV. Applicants have demonstrated herein, that sulfated heparin polysaccharides, in general, inhibit HSV cellular attachment, however, Applicants have demonstrated unexpectedly, that use of heparin polysaccharides contacted with 3-OST-3 provide superior inhibition, as compared to polysaccharides sulfated via other means. Inhibition correlated with 3-OST-3 sulfated polysaccharide binding to HSV gD.

Thus, Lukas in combination with Casu, or Rosenberg, further in view of Lycke, all fail to teach or render obvious, the instant invention, that 3-OST-3 treated heparin sulfate polysaccharides inhibit HSV infection. Accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner rejected claims 1, 20, 23 and 24 as being rendered obvious in view of Larm (WO 98/05341) further in view of Casu (WO 98/42754) or Rosenberg (WO 99/22005) and Lycke et al (J. Gen. Virol., 1991).

The Examiner alleged that Larm teaches that sulfated polysaccharides such as heparin inhibit HSV-1 infection. Applicants have, as stated above, demonstrated that sulfated heparin polysaccharides, in general, inhibit HSV cellular attachment, however, Applicants demonstrated unexpectedly, that use of heparin polysaccharides contacted with 3-OST-3 provide superior inhibition, as compared to polysaccharides sulfated via other means.

Applicants, in contrast to all other art presented herein, have shown that heparin sulfates alone are very effective in inhibiting HSV infection, if the heparin sulfate

polysaccharide preparation is enriched for polysaccharides produced as a result of 3-OST-3 sulfation. Polysaccharides produced as a result of 3-OST-1 contact with heparin sulfate are not as effective in inhibiting HSV infection.

It would not have been obvious, therefore, to one having ordinary skill in the art, to administer a polysaccharide as taught by the present invention, namely a 3-OST-3 sulfated polysaccharide for the inhibition of HSV infection. Lukas, Larm or Lycke did not teach that 3-OST-3 sulfated polysaccharides would be effective in inhibiting HSV infection, nor did Casu or Rosenberg specifically teach the use of such polysaccharides for the enhanced inhibition of infection, as compared to what is seen with, for example 3-OST-1 sulfated heparin polysaccharides.

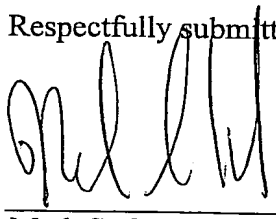
Therefore, Applicants respectfully assert that all claims are novel and unobvious, in view of the cited references, as are dependents therefrom. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections to the claims.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 05-0649.

Respectfully submitted,



Mark S. Cohen
Attorney for Applicant(s)
Registration No. 42,425

Dated: March 25, 2004

Eitan, Pearl, Latzer & Cohen Zedek, LLP
10 Rockefeller Plaza, Suite 1001
New York, NY 10020
Telephone: (212) 632-3494
Fax: (212) 632-3489